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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,038	07/10/2000	Antonio J. Grillo-Lopez	P1752R1	9334

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Attn Wendy Lee
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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/613,038	GRILLO-LOPEZ ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-16,22,28 and 32-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-16,22,28 and 32-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____. .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 1/28/05, is acknowledged.

2. Claims 1, 6-16, 22, 28 and 32-60 are pending and under examination in the instant application.

3. Applicant is advised that should claims 43, 50 and 52-53 be found allowable, claims 51 and 57-60 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

4. Applicant's statement, filed 1/28/05 in conjunction with a deposit of the hybridoma in U.S. Patent No. 6,682,734 under the provisions of the Budapest Treaty, satisfies the requirement for the deposit of the biological material 2B8 (HB 11388) under 35 USC § 112, first paragraph.

5. In view of the amendment filed on 1/28/05, only the following rejections are remained.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 6, 11-16, 22, 28, 34-39, 43-48, 50-55 and 57-60 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/04281 (IDS Ref. No. 31) for the same reasons set forth in the previous Office Action mailed 7/28/04.

The `281 publication teaches and claims an improved method of treating immune cell mediated diseases comprising administering to a patient (i.e., human) (page 7, lines 16-21) a therapeutic protein such as a monoclonal antibody (see published claim 1), wherein the immune cell is a B-cell (see published claim 19), wherein the B-cell antigen is human CD20 (see published claim 23), wherein the therapeutic protein is a monoclonal antibody to human CD20 (see published claim 25), wherein the dose is given intravenously (published claim 15) and wherein the B-cell mediated disease is graft verses host disease (see published claim 21 in particular). The `281 publication further teaches that the therapeutic proteins are useful in the treatment of transplanted organ rejection such as heart, lung, kidney, cornea, bone marrow, skin, etc (see page 10 lines 1-3 in particular). In addition, the `281 publication teaches that the monoclonal antibody can be chimeric, human or humanized (see page 7, lines 5-14 in particular). The `281 publication teaches that the administration can be accomplished subcutaneous (see page 7, under Route of

Administration) or intravenously (see page 1 line 14-15, page 20, under intravenous administration and tables 1-5). The `281 publication further teaches a dosing regimen of 10mg/kg (see page 3, line 18) or 40, 80, 100, 120, 140 mg/bi-week (see page 10, lines 30-3 and tables 1-5). The `281 publication teaches that the improvement method comprises administering a dose of therapeutic protein (i.e. anti-CD20), followed by a second administration of said therapeutic protein, wherein the systemic exposure of said therapeutic protein from the second administration is at least 50% greater than the systemic exposure from a first (see published claim 1). The `281 publication teaches prophylatic use in transplanted organ rejection (see page 10, lines 13-14 in particular).

While the prior art teachings may be silent as to the "the circulating levels of B cells in the human are reduced to block said immune response" per se; the WO `281 publication exemplifies the reduce circulating levels of B cells using the same antibody. Therefore "the circulating levels of B cells in the human are reduced to block said immune response" is considered inherent properties.

Further, while the prior art teachings may be silent as to the "wherein in each administration of the antibody is by intravenous injection", the term "comprising administering" is an open-ended, it would open up the claim to include each administration. The court has held that the use of "comprising" in the claim language meant that the whole plasmid was encompassed by the claim. (*In re Crish*, Fed. Cir., No. 04-1075, 12/21/04).

Claims 13-15, 50, 52-53, 59-60 are included because the specific doses taught by the '281 publication anticipate the claimed rages.

Claims 43, 44, 51, and 58 are included because the reference dosages are substantially less than 375 mg/m^2.

Claim 22 is included because the `281 publication teaches a prophylatic use in transplanted organ rejection, therefore it will be immediately apparent to administer the antibody to the patient before the patient is exposed to the graft in the prophylatic use of the transplanted organ rejection.

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 1/28/05, have been fully considered, but have not been found convincing.

Applicant submits that the (Davis et al) WO`280 publication cannot meet the standards required for anticipation under 102(b) for the currently presented claims because it does not disclose a method meeting all of the limitations of the pending claims, as amended. Applicant argues that claim 1 requires use of an antibody that binds to the CD20 antigen on human B lymphocytes in the prevention of rejection of an allogeneic graft in a human. Claim 28 requires use of an antibody that binds to the CD20 antigen on human B lymphocytes to treat graft versus host or

host versus graft disease in a human. Applicant contends that there is no disclosure within the Davis publication that anti-CD20 antibodies can or should be used in the two treatment settings specified in the claims. Applicant contends that the graft rejection and graft-versus-host diseases are merely listed as two of a wide variety of disorders and illnesses that may be treated by administration of antibodies to "immune cell antigens" (in a generic sense). Further, Application argues that this teaching is not a teaching that is sufficient under the standard of 102(b), because there is no suggestion of use of antibodies that bind to the CD20-antigen, to treat graft rejection and graft-versus-host disease.

Contrary to Applicant argument the WO `289 publication meet the standards required for anticipation under 102(b) because the prior art meets the claimed limitation. Published claim 1 recites a method for treating immune cell mediated diseases comprising administering a saturating dose of a monoclonal antibody, while claim 19 recites the immune cell is a B-cell, claim 25 recites the therapeutic protein is a monoclonal antibody to human CD20, claim 31 recites the B-cell mediated disease is *graft verses host disease*. The graft verses host disease are claimed in the WO `280 publication rather than "merely listed as two of a wide variety of disorders and illnesses that may be treated by administration of antibodies to "immune cell antigens" (in a generic sense)".

Applicant further argues that the WO `280 publication is generally directed to methods for increasing the systemic exposure of therapeutic proteins which bind to selected antigens on the surface of immune cells. Applicant submits that the `280 publication teach the systemic exposure of therapeutic proteins which bind to selected antigens on the surface of immune cells "is increased by firs providing (or administering) a saturating dose of the therapeutic protein followed by a second administration of such therapeutic protein, which is given subcutaneously, whereby the systemic exposure of the second administration is at least 50% greater than an equivalent subcutaneous dose administered without the benefit of the saturating dose. Applicant continue to argue that the `280 publication teach that a "saturating dose" is "the amount of therapeutic protein necessary to completely bind a selected immune cell antigen in the lymphatic system such that no appreciable binding of the therapeutic protein to the immune cell antigen occurs upon subsequent administration(s)of the therapeutic protein.

However, it is clear that both the `280 publication and Applicant administer the same composition comprising the same antibody to the same patient to achieve the same results. The prior art and applicant have suggested different administration routes but both the `280 and Applicant claiming the administration of the claimed antibody intravenously. Therefore, the claimed limitations are anticipated.

Applicant argues that the `280 publication does not teach that administration of a first dose of antibody will or even can be a "therapeutically effective amount." Instead, the `280 publication teach that administration of a "saturating dose" of an antibody should be followed by administration of a second subcutaneous dose of that antibody. Applicant concludes that since the `280 publication does not teach a first administration of therapeutically effective dose of antibody that binds to the CD20 antigen, then the `280 cannot anticipate the present claims.

Again both the `280 publication and Applicant administer the same composition comprising the same antibody to the same patients to achieve the same results. The `280 publication teaches that the "saturating dose" for a human anti-CD4 monoclonal antibody will typically be in the range of 0.5-5 mg/kg (see page 4, line 26). Instant claim 43 recites the antibody is substantially less than 375 mg/m2 (i.e. for hypothetical 75kg would be less than 8.55 mg/kg ($375mg/m^2*1.71m^2$)/75kg)). The 5 mg/kg is less than 8.55mg/kg. Said dosage is used because it is an effective B cell depleting dosage and per applicants comments regarding "saturating dose", the amount of therapeutic protein necessary to completely bind a selected immune cell antigen in the lymphatic system. Therefore, the reference anticipated the claimed invention. .

Applicant asserts that the `280 publication does not teach a method where antibodies to the CD20 antigen are used to block an immune response to a graft or the treat graft-versus-host disease. However, the published claims 1, 25 and 31 reads on the claimed method of the instant application.

Applicant further submits that the Examiner limits claim 1 to methods where the immune-cell related disorder is a B-cell disorder. However, published claim 1 does not limit the disorder to a B-cell disorder but rather to immune cell mediated diseases.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 7-10, 28, 32, 40, 41, 45-46, 49 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of Business Wire (2/24/1998) for the same reasons set forth in the previous Office Action mailed 7/28/04.

The teachings of WO 98/04281 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the antibody comprises rituximab in claims 7,40, 49 and 56, conjugated with a cytotoxic agent in claim 8, Y2B8 in claims 10, 32, and 41 wherein the cytotoxic agent is a radioactive compound in claim 9.

The Business Wire article teaches IDEC-Y2B8, Rituxan™ (Rituximab), is a monoclonal antibody tightly conjugated to the radioisotope yttrium-90, which targets the CD20 antigen on mature normal and malignant B cells. Further the article teaches that the MX-DTPA used to create IDEC-Y2B8 exhibits excellent in vivo retention of yttrium. Further, studies in mice have shown minimal loss of the radioisotope from the conjugate and not significant accumulation of yttrim in bone. The article further teaches that IDEC Pharmaceuticals focuses on developing targeted therapies for the treatment of cancer and autoimmune diseases, IDEC's antibody products act chiefly through immune system mechanisms, exerting their effect by binding to specific, readily targeted immune cells in the patient's blood or lymphatic systems (see the entire article).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the Y2B8 antibody as taught by the Business Wire article.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because IDEC-Y2B8 exhibits excellent in vivo retention of yttrium as taught by Business Wire article.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 1/28/05, have been fully considered, but have not been found convincing.

Applicant argues that the `280 publication does not teach either a method for treating graft rejection or of treating graft-versus-host disease using antibodies that bind to the CD20 antigen on human B lymphocytes. Applicant contends that the `280 publication is directed to a generalized method for improving the effectiveness of subcutaneous administration of "immune-cell" specific antibodies to treat "immune cell" mediated diseases. Applicant further submits that the `280 publication teaches a method requiring a particular sequence of steps. Further Applicant asserts that the `280 publication provides only a generalized teaching of use of its improved methods in treating a wide variety of "immune cell mediated diseases" using a wide variety of types of antibodies that target or bind an antigen expressed on the surface of immune cells. Applicant contends that the deficiencies of the `280 publications relative to the present claims are not remedied by the teaching of the Business Wire article. Instead, the Business Wire

article merely reports on initiation of a Phase III trial incorporating both IDEC Pharmaceutical's treatments for relapsed or refractory B-cell non-Hodgkin's lymphoma, IDEC-Y2B8, nad the recently approved immunotherapy, Rituxan. Applicant further argues that there is no discussion in the Business Wire article cited by the Examiner of use of antibodies to the CD20 antigen to treat graft rejections or graft-versus-host disease. Applicant submits that the ordinary artisan would not look to Business Wire for guidance in altering the methods and disclosure of the `280 publication either to select an antibody to CD20 to block immune responses to allogeneic grafts or to treat graft versus host disease, or to devise a new treatment regiment where upon each administration of the antibody, circulating levels of B cells would be reduced in the patient to exhibit the desired therapeutic effect.

However, both Davis et al (`280 publication) and applicant administer the same composition comprising the same antibody to the same patient to achieve the same results. Applicant appears to suggest a different administration steps. However, the `280 publication administration step reads on Applicant's administration step of the same antibody to the same patients to treat GVH disease. The Business Wire article provides clear motivation to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the Y2B8 antibody since IDEC-Y2B8 exhibits excellent in vivo retention of yttrium as taught by Business Wire article.

10. Claims 1, 8-10, 28, 33 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of U.S. Pat. No. 6,498,181 for the same reasons set forth in the previous Office Action mailed 7/28/04.

The teachings of WO 98/04281 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the antibody is conjugated with a cytotoxic agent in claim 8, ^{131}I-B1 in claims 10, 33, and 42 wherein the cytotoxic agent is a radioactive compound in claim 9.

The `181 patent teaches ^{131}I labeled anti-B1 (Bexxar) mAb, raised to the CD-20 antigens that are expressed on the surface of mature B-cells, is one example of a radiolabeled mAb that has seen successful in treating follicular non-Hodgkins lymphoma in recent clinical trials (see co. 9, lines 19-30 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the $^{131}$I-B1 antibody as taught by the `181 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because ^{131}I-B1 has seen successful in recent clinical trials as taught by `181 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 1/28/05, have been fully considered, but have not been found convincing.

Applicant argues that the `280 publication does not teach what the Examiner has suggested. Applicant submits that the `280 publication does not disclose a method of blocking an immune response to a graft or treatment of graft versus host disease using antiboies that bind to the CD20 antigen, wherein those antibodies, upon each administration, deplete circulating B cell populations to exhibit the desired therapeutic effect. Application submits that the `280 publication is directed to generalized methods of enhancing availability of administered antibodies. Applicant contends that the `181 patent does not cure the deficiencies of the Davis reference. Applicant submits that the `181 patent is directed to methods of treating cancer. Applicant submits that the ordinary artisan would not look to the `181 patent for guidance in blocking an immune response to an allogeneic graft or treating GVH or HVG because the `181 patent is directed to the use of the Bexxar anti-B1 monoclonal antibody in the treatment of cancerous conditions, specially non-Hodgkins lymphoma. Applicant contends that the present application specifically exclude therapy of malignant or cancerous conditions.

It appears that applicant and the examiner differ on interpretation of both the claimed methods and the prior art. Also, applicant relies upon an asserted and claimed mechanism of action but does not provide objective evidence that the prior art teaching of treating the same graft-versus-host patient populations with the same compositions to achieve the same therapeutic effect differs from the claimed methods. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the $^{131}$I-B1 antibody because $^{131}$I-B1 has seen successful in recent clinical trials as taught by `181 patent.

11. It is noted that New Grounds of Rejection are set forth herein.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 6-16, 22, 28, 32-44, 50-51 and 57-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The recitation "a first administration" in claims 1 and 28 is ambiguous because a first administration indicates that there are additional administrations, however, the claim only recites a first administration. It is not clear whether the first administration is the only administration or there are additional administrations of the antibody.

B. The "mammal" recited in claims 13 and 22 has no antecedent basis in base claim 1, base claim 1 only recites human.

C. The "mammal" recited in claims 50 and 57 has no antecedent basis in base claim 45, base claim 45 only recites human.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1, 6-16, 22, 28, 32-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "wherein after a first administration" claimed in claims 1 and 28 and the phrase "wherein each administration of the antibody" claimed in claims 45-46, represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 1/28/05 points to the specification at page 8, line 24 to page 9, line 4page 41, line 25 to page 42, line 22 for support for the newly added limitations "wherein after a first administration" as claimed in claims 1 and 28 and "wherein each administration of the antibody" as claimed in claims 45-46. However, the specification does not provide a clear support for such limitations. However, Page 8, line 24 to page 9, line 4 of the instant specification only discloses that the antagonist upon binding to CD20, destroys or depletes B cells, no reference to a first administration of the antibody was found. Further, page 42, lines 16-24 only disclose the route of the administration is given by injections, most preferably intravenous injection, no reference that each administration of the antibody is by intravenous injection. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
April 15, 2005

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